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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,792	02/05/1999	ALDO T. IACONO	P32130	4164

21003 7590 12/05/2006

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/244,792	IACONO, ALDO T.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21,24-26,29-31 and 33-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21,24-26,29-31 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 28, 2006 has been entered.

Claim Rejections 35 U.S.C. 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 19-22, 25-26, 29-31, 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldrep et al. (US 5,958,378) and Fuji et al. (US 6,197,829), in view of Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS)

4. Waldrep et al. and Fuji et al. teaches that cyclosporine are old and well known in combination with various pharmaceutical carriers and excipients in various dosage forms, particularly, aerosol dosage form. These medicaments are taught as useful as immunosuppressant for treating or preventing graft rejections, inflammation and other immunological mediated conditions such as graft rejections of lung, heart, and other organs, asthma, autoimmune disease, such as rheumatoid arthritis, systemic lupus erythematosis. Specific liposome aerosol dosages are disclosed. The aerosol dosage may be either is solution or in powder forms. See, particularly,

the abstract, col. 4, line 22 to col. 5, 64, the examples, col. 13, lines 3-60, and the claims in Waldrep et al. and, column 7, lines 40 to col. 8, lines 59, and the claims in Fuji et al. Cyclosporine is particularly known to be used with other immunosuppressant for treatment of those disorders. See, the claims in Fuji.

5. Waldrep et al. and Fuji et al. do not teach expressly the various dosage forms, or the dosage levels herein claimed, or the particular time of administration as herein claimed.

However, Adjei et al. teaches that pulmonary delivery of peptide and protein biotherapeutics, such as cyclosporine, by aerosol is well known in the art. Both suspension (solid particle) and solution aerosol formulas are known in the art. propellants are normally used with the aerosol composition. See, particularly, Col. 1, lines 15 to col. 2, line 65, and the examples. Knight et al. teaches that cyclosporine aerosol dosage may be in the form of powder. See, particularly, example 2 therein. Gordon et al. disclosed that dry powder is a well-known form for pulmonary aerosol drug delivery. See, particularly, col. 1, lines 15-67, and the claims. Aldo et al. teaches a cyclosporine composition for aerosol delivery consisting of cyclosporine, a solvent and a propellant and the method of using the same for treating lung graft rejections. See, the whole article, particularly, page 1691, col. 2, the paragraph subtitled "Drug preparation, aerosol generation, and therapy."

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treating the patients of organ transplantation, either lung, or non-lung transplantation prior to the development of symptoms associated the transplant rejection with the aerosol composition comprising cyclosporine and another

immunosuppressant, or treating other patients with inflammatory condition, immunological mediated conditions such as asthma, or rheumatoid arthritis.

A person of ordinary skill in the art would have been motivated to treating the patients of organ transplantation, either lung, or non-lung transplantation prior to the development of symptoms associated the transplant rejection with the aerosol composition comprising cyclosporine and another immunosuppressant, or treating other patients with inflammatory condition, immunological mediated conditions such as asthma, or rheumatoid arthritis because cyclosporine are known to be useful for organ transplantation patients and are known for treating inflammatory disease or immunological mediated conditions herein, and are particularly known to be delivered through pulmonary delivery. Further, the cited prior art as a whole teach various aerosol formulation of cyclosporine, encapsulated, or un-encapsulated as an improvement over simple aerosol employment of powdered active ingredient, and the aerosol cyclosporine as useful for an anti-inflammation, anti-rejection medicaments. The skilled artisan would have possessed all conventional administration regimens, and seen the selection of one or another as the simple selection from among obvious alternatives. Further, optimization of a result effective parameter, e.g., effective amount of a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Further, as disclosed in the prior art, the employment of the particular method disclosed therein is to improve the old and well-known aerosol delivery method. Therefore, employ the compound only without the further employment of carrier as herein recited would have been within the purview of the skilled artisan. Further, as to recitation of "chronic refractory" in claim 19, it is noted that a method known for preventing

transplantation rejections would reasonably expected to prevent the development of rejections, either chronic or acute.

6. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Waldrep et al. (US 5,958,378) and Fuji et al. (US 6,197,829), in view of Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS) for reasons discussed above, and in further view of Armistead et al. (US 5,665,774).

7. Waldrep et al.. (US 5,958,378) and Fuji et al. (US 6,197,829), Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS) as a whole do not expressly teach the further incorporation of an anti-inflammatory agents for the preventing graft rejections.

8. However, Armistead et al. teaches that steroid is useful in treating or preventing graft rejections. See, particularly the claims.

9. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made to co-administer the cyclosporine composition with a steroid for preventing graft rejection.

Response to the Arguments

10. Applicants' amendments, remarks and exhibits submitted August 28, 2006 have been fully considered, but are not persuasive with respect to the rejections set forth above.

As to the arguments about the combination of cyclosporine with other immunosuppressant, such arguments are moot in view of the new ground of rejections,

particularly the Fuji et al. references. Further, it is noted the limitation of combination with other immunosuppressant is only in claim19 and its dependent claims.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., non-liposome) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

11. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Considering the cited references as whole, one of ordinary skill in the art would have viewed the employment of aerosol form of cyclosporine for treatment or prevention of transplant rejections or other inflammatory conditions or immunological mediated conditions as obvious.

12. Applicants argue that there is no teaching or suggestion that cyclosporine be administered prior to the development of rejections. The arguments are untenable as the references suggest immunosuppressant, such as cyclosporine, are useful both for treatment and prevention of graft rejection. Therefore, prophylactic treatment of transplantation patients with cyclosporine would have been obvious to one of ordinary skill in the art.

13. Applicants' remarks regarding Iacono lack probative force. One of ordinary skill in the art would not expect that each and every therapeutics be perfect. Cyclosporine may not be

perfect, but have been taught to be useful for graft rejection, inflammatory conditions, and immunological mediated conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617